

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
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## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference <b>27909</b>		Date of mailing (day/month/year) <b>23 NOV 2004</b>
International application No. <b>PCT/IL04/00453</b>		FOR FURTHER ACTION See paragraph 2 below
International filing date (day/month/year) <b>27 May 2004 (27.05.2004)</b>	Priority date (day/month/year) <b>27 May 2003 (27.05.2003)</b>	
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): A61K 31/66; C07F 9/02 and US Cl.: 514/114; 558/169, 170, 172.</b>		
Applicant <b>VASCULAR BIOGENICS, LTD</b>		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT. Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 872-9306	Authorized officer Robert Shiao <i>RS 11/2/04</i> Telephone No. (571) 272-1600 <i>RD Sar</i> <i>10/22/04</i>
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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/IL04/00453

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE  
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International application No.  
PCT/IL04/00453

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims 52-90	YES
	Claims 1-51	NO
Inventive step (IS)	Claims 1-90	YES
	Claims NONE	NO
Industrial applicability (IA)	Claims 1-90	YES
	Claims NONE	NO

**2. Citations and explanations:**

Claims 1-51 lack novelty under PCT Article 33(2) as being anticipated by (1)

Watson et al. publication, Journal of Biological Chemistry, 1997, 272(21), 13597-13607; (2) Shaw et al. publication, J. of Clinical Investigation, 2000, 105(12), 1731-1740, also see CAS: 133:162827.

Applicants claim a compound/composition of formula (I) in claim 1 as agents treating inflammatory disease.

Watson et al. disclose a compound, see page 13603, Fig 6A, clearly anticipates the claimed compounds of formula (I), wherein the variable n is 3, the variable B1, B2, or B3 independently represents oxygen (i.e., O); the variable A1 or A2 independently C=O, X1 and X2 represent formula (II), and the variable m is 1 or 15, and the variable Z is W=CR"- when m is 1 of -A2-X2- of formula (I), and W is O, R" is hydroxy; or Z is hydrogen when m is 15 of -A1-X1- of formula (I), the variable R1, R'1, R2, R3, R'3, Ra, R'a, Rb, or R'b independently represent hydrogen; the variable Y represents phosphoryl choline.

Shaw et al. disclose a compound 3,5,9-trioxa-4-phosphapentacosan-1-aminum, 7-[(1,5-dioxopentyl)oxy]-4-hydroxy-N,N,N-trimethyl-10-oxo, clearly anticipates the claimed compounds of formula (I), wherein the variable n is 3, the variable B1, B2, or B3 independently represents oxygen (i.e., O); the variable A1 or A2 independently C=O, X1 and X2 represent formula (II), and the variable m is 1 or 15, and the variable Z is W=CR"- when m is 1 of -A2-X2- of formula (I), and W is O, R" is hydrogen; or Z is hydrogen when m is 15 of -A1-X1- of formula (I), the variable R1, R'1, R2, R3, R'3, Ra, R'a, Rb, or R'b independently represent hydrogen; the variable Y represents phosphoryl choline.

Claims 1-90 meet the criteria set out in PCT Article 33(3). Claims 1-90 are neither anticipated nor rendered obvious over the art of record, and therefore are allowable. This invention relates to oxidized lipid or compound/composition of formula (I) as agents treating inflammatory disease. The closest prior art is Baldo et al. US 5,061,626, disclose antigenic analogues platelet activating factor. The difference between prior art and instant claims is that instant oxidized lipid or compounds of formula (I) is not used for the treatment of inflammatory disease. Suggestion for modification of above reference to obtain the instant methods of use, has not been found.

Claims 1-90 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.